

In the Specification:<sup>1</sup>

Insert the following paragraph on page 1, after the title:

This application is a continuation of International Application No. PCT/US02/02171, filed January 25, 2002, which claims benefit of U.S. Provisional Application Nos. 60/264,398, filed January 26, 2001; 60/266,106, filed February 2, 2001; 60/265,984, filed February 3, 2001; and 60/270,466, filed February 21, 2001. The teachings of these prior applications are incorporated herein in their entirety.

Replace the paragraph starting at page 49, line 29 with the following paragraph:

In another embodiment, an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein (such as HIV-1<sub>SF162</sub> gp120 protein) and that has HIV-1 neutralizing activity is provided, wherein said antibody or antigen-binding portion thereof recognizes an epitope (preferably a linear epitope) on a V1/V2 domain of HIV-1 gp120, such as HIV-1<sub>SF162</sub> gp120, wherein said epitope is

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<sup>1</sup> An "Appendix A: Specification Amendments" is enclosed herewith showing the amendments to the specification. In the Appendix, additions are underscored and deletions are bracketed.

dependent on the presence of a sequence in the V2 domain. In a more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof recognizes an epitope (preferably a linear epitope) on a V2 domain of HIV-1 gp120, such as HIV-1<sub>SF162</sub> gp120. In another preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof has HIV-1 neutralizing activity. In a more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof has HIV-1<sub>SF162</sub> neutralizing activity. In another preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120, such as HIV-1<sub>SF162</sub> gp120, and the antibody or antigen binding portion thereof has HIV-1<sub>SF162</sub> neutralizing activity. In a preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof specifically binds to at least three R5 clade B HIV-1 gp120 proteins. In a preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof specifically binds to a peptide consisting of SEQ ID NO: 4. In another preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof does not specifically bind to a gp120 of HIV-1 IIIB, or related clones, such as HXB2, HXB2d and BH10. In a more

preferred embodiment, said human antibody described in this paragraph or antigen-binding portion thereof is a human monoclonal antibody. In an even more preferred embodiment, said human Mab is Mab 8.22.2, secreted by a hybridoma designated by ATCC Accession Number PTA-4007.

Replace the paragraph starting at page 51, line 7 with the following paragraph:

In another embodiment of this invention, an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120 is provided, wherein, preferably, said antibody binds to an epitope in the V3 region of HIV-1<sub>SF162</sub> gp120, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO:9 (V3 amino acids 1-20 of gp120 of HIV-1 MN strain). In a more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof specifically binds to a HIV-1 gp120 protein (such as HIV-1<sub>SF162</sub> gp120 protein). In a more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof binds to an epitope (linear or conformational) on the V3 region of HIV-1<sub>SF162</sub> gp120. In another preferred embodiment, said antibody described in this

paragraph or antigen-binding portion thereof has HIV-1 neutralizing activity. In a more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof has HIV-1<sub>SF162</sub> neutralizing activity. In an even more preferred embodiment, said antibody described in this paragraph or antigen-binding portion thereof is human monoclonal antibody 8.27.3, secreted by a hybridoma designated by ATCC Accession Number PTA-3009 or Mab 8E11/A8, secreted by hybridoma designated by ATCC Accession Number PTA-4012. As shown in **Example 1**, Mab 8.27.3 and mab 8E11/A8 did not specifically bind MN V3 1-20 (SEQ ID NO: 9). As shown in **Figure 9**, Mab 8.27.3 was shown to have a SF162 HIV-1 virus neutralizing activity of about 0.11 µg/ml and Mab 8E11/A8 was shown to have a SF162 HIV-1 virus neutralizing activity of about 2.6 µg/ml. As shown in **Figure 2** and **Example 1**, Mabs 694 and 447-52D (described in U.S. patent 5,914,109), included here for comparison purpose, specifically bound to MN V3 1-20 (SEQ ID NO: 9). In contrast, human monoclonal antibodies 8.27.3 and 8E11/A8, made according to the above-identified procedure (see also Example 1), did not specifically bind MN V3 1-20 (SEQ ID NO: 9) or MN V3 21-40 (SEQ ID NO: 11), but did bind to a larger peptide containing all 33 amino acids of the MN V3 loop (TRPNYNKRKRIHIGPGRAFYTTKNIIGTIRQAH) (SEQ ID NO: 7).

Mab 8.27.3 did not bind MN V3 11-30 (SEQ ID NO: 10), whereas Mab 8E11/A8 did.

Replace the paragraph starting at page 91, line 10 with the following paragraph:

Soluble, rgp120s from the R5-tropic clade B primary isolates HIV<sub>SF162</sub> (Cheng et al. (1989) Proc. Natl. Acad. Sci. U S A. 86:8575-8579) and HIV<sub>JR-FL</sub> (Koyanagi, Y. et al. (1987) Science 236:819-822) were secreted from HEK293 (Graham et al. (1977) J. Gen. Virol. 36:59-72) cell lines stably expressing the recombinant proteins from pcDNA3.1zeo (Invitrogen). Coding sequences for these gp120s with were prepared by PCR from the molecular clones and fully sequenced. The sequence for rgp120<sub>JR-FL</sub> was optimized at its initiation codon (Kozak (1989) J. Cell Biol. 108:229-241) and had a His6 affinity tag (SEQ ID NO: 28) embedded in a run of Ala and Gly residues at its C-terminus.

Replace the paragraph starting at page 117, line 24 with the following paragraph:

The following hybridoma (which is mouse hybridoma) expressing the antibody as indicated below --  
cell line 8.22.2 (Mab 8.22.2): ATCC Accession No. PTA-4007,

was deposited with the American Type Culture Collection ("ATCC"), 10801 University Boulevard, Manassas, VA 20110-2209, USA, on January 24, 2002, and given the above-indicated ATCC Accession Number.

Replace the paragraph starting at page 118, line 5 with the following paragraph:

The following hybridoma (which is a mouse hybridoma) expressing the antibody as indicated below -- cell line 8E11/A8 (Mab 8E11/A8): ATCC Accession No. PTA-4012, was deposited with the American Type Culture Collection ("ATCC"), 10801 University Boulevard, Manassas, VA 20110-2209, USA, on January 25, 2002, and given the above-indicated ATCC Accession Number.

Replace the paragraph starting at page 119, line 12 with the following paragraph:

All publications, patents and patent applications cited in this specification are herein incorporated by reference as if each individual publication, patent or patent application were specifically and individually indicated to be incorporated by reference.